I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING SENT TO THE ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C., 20231, VIA FACSIMILE AT FACSIMILE NO. 703-305-5433 ON:

Date: March 19, 1997 By: Gerald F. Swiss

#7/fm
3-20-97

Patent
Attorney's Docket No. 018413-002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	BOX AF
RICHARD J. GREFF, et al	)	
	)	Group Art Unit: 1511
Application No.: 08/507,863	)	Examiner: P. Niland
Filed: July 27, 1995	)	
For: NOVEL COMPOSITIONS FOR USE IN EMBOLIZING BLOOD VESSELS	)	

DECLARATION OF RICHARD GREFF PURSUANT TO 37 C.F.R. §1.132

The Assistant Commissioner for Patents
BOX AF
Washington, D.C. 20231

Sir:

I, RICHARD GREFF, hereby declare:

1. I am a joint inventor for the above-noted application.

2. I have a Ph.D. in Polymer Chemistry from Polytechnic University, New York in 1970 and have over 25+ years experience in polymer chemistry including over 2 years of experience in the preparation and use of embolic compositions as set forth in the claims of this application including those comprising tantalum or barium sulfate as the water insoluble contrast agent.

3. I am currently a consultant and, among other clients, I am a consultant with MicroTherapeutics, Inc., assignee of the entire right, title and interest in this application.

4. I am familiar with the final Office Action received in the above-noted application and with the claimed invention which relates to compositions comprising from about 2.5 to about 8 weight percent of a copolymer of ethylene vinyl alcohol, from about 10 to about 40 weight percent of a water insoluble contrast agent selected from the group consisting of tantalum, barium sulfate and tantalum oxide and from about 52 to about 87.5 weight percent of a biocompatible solvent as well as methods for embolizing blood vessels using such compositions.

5. I was present during an interview with Examiner Niland conducted by Gerald F. Swiss, Esq. (Reg. No. 30,113) on March 17, 1997 concerning the final Office Action received in this application wherein Mr. Swiss stated that Example 3 of this application demonstrated that a composition comprising metrizamide (a water soluble contrast agent) failed to provide for a well defined solid precipitate when injected into saline.

6. In fact, Example 3 of this application was based on an experiment conducted under my supervision and direction and the particulars of the composition of this example are found at page 16 of this application.

7. After a review of the results of this experiment and based on my recollection of these results, I hereby confirm that the metrizamide containing composition did not form a well defined solid mass upon injection into saline but, as I observed, a loosely defined precipitate was formed having the consistency of tissue/toilet paper when exposed to water which, within seconds after forming, began to disintegrate/fragment.

8. In comparison and as requested by Examiner Niland during the interview, I conducted the following experiment to determine whether tantalum, a water insoluble contrast agent, provided for different results than the metrizamide containing composition

when employed at the maximum weight amounts for the ethylene vinyl alcohol copolymer and the water insoluble contrast agent as recited in Claim 1.

9. At my instructions, a composition comprising 8 weight percent ethylene vinyl alcohol copolymer (68 mole percent vinyl alcohol, 32 mole percent ethylene), 52 weight percent of dimethyl sulfoxide (DMSO – biocompatible solvent) and 40 weight percent tantalum (water insoluble contrast agent) was prepared.

10 After thoroughly shaking the composition, I partially filled a 1 cc syringe having a 21 gage needle attached thereto with this composition and 0.1 cc of this composition was then injected from the syringe into a saline solution maintained at about 37°C whereupon a coherent mass/precipitate formed immediately. After about 5 minutes, the precipitate was removed from the saline with tweezers and examined manually. The precipitate was soft, spongy and did not break apart with gentle manipulation and no fragments or fines of the polymer or tantalum were found.

11. Based on the above data, I concluded that the composition comprising 8 weight percent ethylene vinyl alcohol copolymer (68 mole percent vinyl alcohol, 32 mole percent ethylene), 52 weight percent of dimethyl sulfoxide (DMSO) and 40 weight percent tantalum formed a well defined solid mass or precipitate upon injection into saline whereas the metrizamide composition of Example 3 did not.

12. Based upon my experience with compositions of this invention comprising barium sulfate as the water insoluble contrast agent, I expect that compositions comprising barium sulfate will behave equivalently as those containing tantalum. Additionally, I have no reason to believe that compositions comprising tantalum oxide as the water insoluble contrast agent will behave differently.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Richard J. Greff

Richard Greff, Ph.D.

Date: 3/19/97